WHAT IS CLAIMED IS:

1. A delayed burst release formulation comprising a core formed as a compressed tablet and an outer coating that surrounds the core;

said core comprising venlafaxine, or a pharmaceutically acceptable salt thereof, at least one burst controlling agent and a disintegrant; and

said outer coating comprising a water insoluble hydrophobic carrier and water-insoluble but hydrophilic particulate matter.

2. The formulation of claim 1, wherein said burst controlling agent comprises a water insoluble polymer, wherein said polymer swells upon contact with fluid and does not form a hydrogel.

3. The formulation of claim 2, wherein said water insoluble polymer is selected from the group consisting of cross-linked polysaccharide, water insoluble starch, microcrystalline cellulose, water insoluble cross-linked peptide, water insoluble cross-linked protein, water insoluble cross-linked gelatin, water insoluble cross-linked hydrolyzed gelatin, water insoluble cross-linked collagen, modified cellulose, and cross-linked polyacrylic acid.

4. The formulation of claim 3 wherein said cross-linked polysaccharide is selected from the group consisting of insoluble metal salts or cross-linked derivatives of alginate, pectin, xantham gum, guar gum, tragacanth gum, and locust bean gum, carrageenan, metal salts thereof, and covalently cross-linked derivatives thereof.

5. The formulation of claim 3 wherein said modified cellulose is selected from the group consisting of cross-linked derivatives of hydroxypropylcellulose, hydroxypropylmethylcellulose, hydroxyethylcellulose, methylcellulose, carboxymethylcellulose, and metal salts of carboxymethylcellulose.

6. The formulation of claim 3, wherein said water insoluble polymer is calcium pectinate.

7. The formulation of claim 3, wherein said water insoluble polymer is microcrystalline cellulose.

8. The formulation of claim 1, wherein said disintegrant is selected from the group consisting of cross-linked polyvinylpyrrolidinone, sodium starch glycolate, cross-linked sodium carboxymethylcellulose, pregelatinized starch, microcrystalline

starch, water insoluble starch, calcium carboxymethylcellulose, magnesium aluminium silicate, and combinations thereof.

9. The formulation of claim 1, wherein said water-insoluble hydrophobic carrier is selected from the group consisting of dimethylaminoethylacrylate/ethylmethacrylate copolymer, ethyl methacrylate/chlorotrimethylammoniumethyl methacrylate copolymer, dimethylaminoethylmethacrylate/methylmethacrylate and butylmethacrylate copolymer, ethylacrylate and methylacrylate/ethylmethacrylate and methyl methylacrylate copolymer; ethylcellulose, shellac, zein, and waxes.

10. The formulation of claim 1 wherein said water-insoluble hydrophobic carrier is ethylcellulose.

11. The formulation of claim 1 wherein said water insoluble hydrophobic carrier is relatively rigid.

12. The formulation of claim 1, wherein said water insoluble particulate matter is selected from the group consisting of a water insoluble polysaccharide, a water insoluble cross-linked polysaccharide, a water insoluble polysaccharide metal salt including calcium pectinate, a water insoluble cross-linked protein, a water insoluble cross-linked peptide, water insoluble cross-linked gelatin, water insoluble cross-linked hydrolyzed gelatin, water insoluble cross-linked collagen, a water insoluble cross linked polyacrylic acid, a water insoluble cross-linked cellulose derivatives, water insoluble cross-linked polyvinyl pyrrolidone, microcrystalline cellulose, insoluble starch, microcrystalline starch and a combination thereof.

13. The formulation of claim 1, wherein said particulate matter is microcrystalline cellulose.

14. The formulation of claim 1, wherein said core further comprises at least one of an absorption enhancer, a binder, a hardness enhancing agent and an excipient.

15. The formulation of claim 14, wherein said binder is selected from the group consisting of starch, polyvinylpyrrolidone, low molecular weight hydroxypropylcellulose, low molecular weight hydroxypropylmethylcellulose, low molecular weight carboxymethylcellulose, ethylcellulose, gelatin polyethylene oxide, acacia, dextrin, magnesium aluminum silicate, and polymethacrylates.

16. The formulation of claim 14, wherein said hardness enhancing agent is microcrystalline cellulose.

17. The formulation of claim 1, wherein said core further comprises a buffering agent.

18. The formulation of claim 17, wherein said buffering agent is selected from the group consisting of an inorganic salt compound and an organic alkaline salt compound.

19. The formulation of claim 1, wherein said core further comprises a filler.

20. The formulation of claim 19, wherein said filler is selected from the group consisting of, starch, lactitol, lactose, an inorganic calcium salt, sucrose, and combinations thereof.

21. The formulation of claim 1, wherein said core further comprises a flow regulating agent.

22. The formulation of claim 21, wherein said flow regulating agent includes at least one of colloidal silicon dioxide and aluminum silicate.

23. The formulation of claim 1, wherein said core further comprises a lubricant.

24. The formulation of claim 23, wherein said lubricant is selected from the group consisting of stearate salts; stearic acid, talc, sodium stearyl fumarate, and glycerol behenate, or a combination thereof.

25. The formulation of claim 1, wherein said outer coating further comprises a plasticizer.

26. The formulation of claim 25, wherein said plasticizer is selected from the group consisting of dibutyl sebacate, polyethylene glycol and polypropylene glycol, dibutyl phthalate, diethyl phthalate, triethyl citrate, tributyl citrate, acetylated monoglyceride, acetyl tributyl citrate, triacetin, dimethyl phthalate, benzyl benzoate, butyl and/or glycol esters of fatty acids, refined mineral oils, oleic acid, castor oil, corn oil, camphor, glycerol and sorbitol or a combination thereof.

27. The formulation of claim 1, wherein said outer coating further comprises at least one of a wetting agent, a suspending agent, and a dispersing agent, or a combination thereof.

28. The formulation of claim 27, wherein said wetting agent is selected from the group consisting of poloxamer, polyoxyethylene ethers, polyoxyethylene sorbitan fatty acid esters, polyoxymethylene stearate, sodium lauryl sulfate, sorbitan fatty acid esters, benzalkonium chloride, polyethoxylated castor oil, and docusate sodium.

29. The formulation of claim 27, wherein said suspending agent is selected from the group consisting of alginic acid, bentonite, carbomer, carboxymethylcellulose, carboxymethylcellulose calcium, hydroxyethylcellulose, hydroxypropylcellulose, microcrystalline cellulose, colloidal silicon dioxide, dextrin, gelatin, guar gum, xanthan gum, kaolin, magnesium aluminum silicate, maltitol, medium chain triglycerides, methylcellulose, polyoxyethylene sorbitan fatty acid esters, polyvinylpyrrolidinone, propylene glycol alginate, sodium alginate, sorbitan fatty acid esters, and tragacanth.

30. The formulation of claim 27, wherein said dispersing agent is selected from the group consisting of poloxamer, polyoxyethylene sorbitan fatty acid esters and sorbitan fatty acid esters.

31. The formulation of claim 1, wherein said coating further comprises a stiffening agent.

32. The formulation of claim 31, wherein said stiffening agent is cetyl alcohol.

33. The formulation of claim 1, wherein the formulation releases substantially no venlafaxine *in vitro* for at least about two hours.

34. The formulation of claim 33, wherein said *in vitro* delayed burst release occurs after at least about 2 hours.

35. The formulation of claim 34, wherein at least about 60% of the venlafaxine is released *in vitro* about one hour after said delayed burst release occurs.

36. A delayed burst release formulation according to claim 1 wherein substantially no venlafaxine is released *in vivo* until said delayed burst release occurs.

37. The formulation of claim 36, wherein said *in vivo* release occurs after at least about 2 hours.

38. The formulation of claim 36, wherein said *in vivo* release occurs after at least about 3 hours.

39. The formulation of claim 36, wherein said *in vivo* release occurs after at least about 4 hours.

40. A method for providing a therapeutically effective amount of venlafaxine to a subject comprising:

administering orally to the subject a delayed burst release formulation comprising a core and an outer coating that surrounds the core;

said core comprising venlafaxine, or a pharmaceutically acceptable salt thereof, a burst controlling agent and a disintegrant; and

said coating comprising a water-insoluble hydrophobic carrier and a hydrophilic particulate matter.

41. The method of claim 40, wherein said core is formed as a compressed tablet.

42. A method for providing enhanced bioavailability of venlafaxine in a subject, comprising:

administering orally to the subject a delayed burst release formulation comprising a core and an outer coating that surrounds the core;

said core comprising venlafaxine, or a pharmaceutically acceptable salt thereof, a burst controlling agent and a disintegrant; and

said coating comprising a water-insoluble hydrophobic carrier and a hydrophilic particulate matter.

characterized in that the *in vivo* blood plasma concentration of venlafaxine is substantially zero for at least about two hours after oral administration.

43. The method of claim 42 wherein said formulation comprises about 30 to about 120 mg of venlafaxine, or a pharmaceutically acceptable salt thereof.

44. The method of claim 43, wherein said formulation comprises about 60 mg of venlafaxin, or a pharmaceutically acceptable salt thereof.

45. The method of claim 44, wherein said formulation provides bioequivalence to Efexor XR 75 mg.

46. The method of claim 44, wherein said formulations provides similar bioavailability in the area under the concentration-time curve to Efexor XR 75 mg.

47. The method of claim 43, wherein said formulation comprises about 120 mg of venlafaxine, or a pharmaceutically acceptable salt thereof.

48. The method of claim 47, wherein said formulation provides bioequivalence to Efexor XR 150 mg.

49. The method of claim 47, wherein said formulation provides similar bioavailability in the area under the concentration-time curve to Efexor XR 150 mg.

50. A method for providing a therapeutically effective amount of venlafaxine to a subject in need thereof, comprising;

administering orally to the subject a delayed burst release formulation comprising a core and an outer coating that surrounds the core;

said core comprising venlafaxine, or a pharmaceutically acceptable salt thereof, a burst controlling agent and a disintegrant; and

said coating comprising a water-insoluble hydrophobic carrier and a hydrophilic particulate matter.

characterized in that the *in vivo* blood plasma concentration of venlafaxine is substantially zero for at least about two hours after oral administration.

51. The method of claim 50, wherein said core is formed as a compressed tablet.

52. The method of claim 51, wherein the outer coating comprises a water insoluble hydrophobic carrier and a water insoluble particulate matter.

53. The method of claim 52, wherein said water insoluble hydrophobic carrier is selected from the group consisting of a ethylcellulose; dimethylaminoethylacrylate/ ethylmethacrylate copolymer, ethyl methacrylate/chlorotrimethylammoniumethyl methacrylate copolymer; dimethylaminoethylmethacrylate/ methylmethacrylate and butylmethacrylate copolymer; ethylacrylate and methyl acrylate/ethyl meth acrylate and methyl methylacrylate copolymer; and acrylic acid esters, ethylcellulose, shellac, zein, and waxes.

54. The method of claim 52 wherein said water-insoluble hydrophobic carrier is ethylcellulose.

55. The method of claim 52 wherein said water insoluble hydrophobic carrier is relatively rigid.

56. The method of claim 52, wherein said water insoluble particulate matter is selected from the group consisting of a water insoluble cross-linked polysaccharide including calcium pectinate, a water insoluble cross-linked protein, a water insoluble cross-linked peptide, water insoluble cross-linked gelatin, water insoluble cross-linked hydrolyzed gelatin, water insoluble cross-linked collagen, a water insoluble cross linked polyacrylic acid, a water insoluble cross-linked cellulose derivatives, water insoluble cross-linked polyvinyl pyrrolidone, microcrystalline cellulose, insoluble starch, microcrystalline starch, and combinations thereof.

57. The method of claim 52, wherein the core further comprises a burst controlling agent and a disintegrant.

58. The method of claim 55, wherein said burst controlling agent comprises a water insoluble polymer, wherein said water insoluble polymer swells upon contact with liquid and does not form a hydrogel.

59. The method of claim 58, wherein said water insoluble polymer is selected from the group consisting of cross-linked polysaccharide, water insoluble starch, microcrystalline cellulose, water insoluble cross-linked peptide, water insoluble cross-linked protein, water insoluble cross-linked gelatin, water insoluble cross-linked hydrolyzed gelatin, water insoluble cross-linked collagen, modified cellulose, and cross-linked polyacrylic acid.

60. The method of claim 59 wherein said cross-linked polysaccharide is selected from the group consisting of insoluble metal salts or cross-linked derivatives of alginate, pectin, xantham gum, guar gum, tragacanth gum, and locust bean gum, carrageenan, metal salts thereof, and covalently cross-linked derivatives thereof.

61. The method of claim 59 wherein said modified cellulose is selected from the group consisting of cross-linked derivatives of hydroxypropylcellulose, hydroxypropylmethylcellulose, hydroxyethylcellulose, methylcellulose, carboxymethylcellulose, and metal salts of carboxymethylcellulose.

62. The method of claim 58, wherein said water insoluble polymer is calcium pectinate.

63. The method of claim 58, wherein the water insoluble polymer is microcrystalline cellulose.

64. The method of claim 52, wherein said water-insoluble hydrophobic carrier is relatively rigid.

65. The method of claim 57, wherein said disintegrant is selected from the group consisting of polyvinylpyrrolidone, sodium starch glycolate, cross-linked sodium carboxymethylcellulose, pregelatinized starch, microcrystalline starch, water insoluble starch, calcium carboxymethylcellulose, magnesium aluminum silicate, and combinations thereof.

66. The method of claim 50, wherein the delayed burst release provides a blood concentration variability of venlafaxine in said subject which varies less than about 20% over a period of at least 4 hours.

67. The method of claim 66, wherein said blood concentration variability is less than about 10%.

68. The method of claim 50, wherein said core further comprises at least one of an absorption enhancer, a binder, a hardness enhancing agent, and an excipient.

69. The method of claim 68, wherein said binder is selected from the group consisting of starch, polyvinyl pyrrolidone, low molecular weight hydroxypropyl cellulose, low molecular weight hydroxypropyl methylcellulose, low molecular weight of carboxymethylcellulose, ethylcellulose, gelatin polyethylene oxide, acacia, dextrin, magnesium aluminum silicate, and polymethacrylates.

70. The method of claim 50, wherein said core further comprises a buffering agent.

71. The method of claim 70, wherein said buffering agent is selected from the group consisting of an inorganic salt compound and an organic alkaline salt compound.

72. The method of claim 50, wherein said core further comprises a filler.

73. The method of claim 72, wherein said filler is selected from the group consisting of starch, lactitol, lactose, inorganic calcium salt, and sucrose, or a combination thereof.

74. The method of claim 50, wherein said core further comprises a flow regulating agent.

75. The method of claim 74, wherein said flow regulating agent is selected from the group consisting of colloidal silicon dioxide and aluminum silicate, or a combination thereof.

76. The method of claim 50, wherein said core further comprises a lubricant.

77. The method of claim 76, wherein said lubricant is selected from the group consisting of stearate salts, stearic acid, talc, sodium stearyl fumarate, glycerol behenate, and combinations thereof.

78. The method of claim 50, wherein said outer coating further comprises a plasticizer.

79. The method of claim 78, wherein said plasticizer is selected from the group consisting of dibutyl sebacate, polyethylene glycol and polypropylene glycol, dibutyl phthalate, diethyl phthalate, triethyl citrate, tributyl citrate, acetylated monoglyceride, acetyl tributyl citrate, triacetin, dimethyl phthalate, benzyl benzoate, butyl and/or glycol esters of fatty acids, refined mineral oils, oleic acid, castor oil, corn oil, camphor, glycerol sorbitol, and combinations thereof.

80. The method of claim 50, wherein said outer coating further comprises a stiffening agent.

81. The method of claim 80, wherein said stiffening agent is cetyl alcohol.

82. The method of claim 50, wherein said outer coating further comprises at least one of a wetting agent, a suspending agent, a dispersing agent, or a combination thereof.

83. The method of claim 82, wherein said wetting agent is selected from the group consisting of poloxamer, polyoxyethylene ethers, polyoxyethylene sorbitan fatty acid esters, polyoxymethylene stearate, sodium lauryl sulfate, sorbitan fatty acid esters, benzalkonium chloride, polyethoxylated castor oil, and docusate sodium.

84. The method of claim 82, wherein said suspending agent is selected from the group consisting of alginic acid, bentonite, carbomer, carboxymethylcellulose, carboxymethylcellulose calcium, hydroxyethylcellulose, hydroxypropylcellulose, colloidal silicon dioxide, dextrin, gelatin, guar gum, xanthan gum, kaolin, magnesium aluminum silicate, maltitol, medium chain triglycerides, methylcellulose, polyoxyethylene sorbitan fatty acid esters, polyvinylpyrrolidone, propylene glycol alginate, sodium alginate, sorbitan fatty acid esters, and tragacanth.

85. The method of claim 82, wherein said dispersing agent is selected from the group consisting of poloxamer, polyoxyethylene sorbitan fatty acid esters and sorbitan fatty acid esters.

86. The method of claim 50, wherein said formulation provides a delayed burst release after at least three hours resulting in dispersion mainly through the colon of the active ingredient into the blood stream as a result of colon absorption over a period of at least 24 hours.

87. The method of claim 86, wherein said outer coating comprising a water insoluble hydrophobic carrier and water-insoluble but hydrophilic particulate matter, contained in the carrier, that forms channels in said outer coating upon contact with the colon medium, wherein said channels imbibe liquid and cause said at least one burst controlling agent to burst said coating, thereby enabling the delayed burst release of venlafaxine after at least three hours followed by dispersion of venlafaxine into the blood stream mainly through the colon over a period extending over at least twenty-four hours.

88. A formulation for release of venlafaxine mainly in the colon of a subject, comprising:

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AMENDED CLAIMS

[received by the International Bureau on 26 July 2004 (26.07.04); original claims 89-93 have been added.

(a) a core that comprises an effective amount of venlafaxine, wherein said core contains at least one burst controlling agent and a disintegrant, and wherein said core is formed as a compressed tablet; and

(b) an outer coating over said core, said outer coating comprising a water insoluble hydrophobic carrier and water-insoluble but hydrophilic particulate matter, contained in the carrier, that forms channels in said outer coating material upon contact with the colon medium, wherein said channels imbibe liquid and cause said at least one burst controlling agent to burst said coating, thereby providing delayed burst release of venlafaxine after at least three hours followed by dispersion of venlafaxine into the blood stream mainly through the colon over a period extending over at least twenty-four hours.

89. A method for providing a therapeutic blood plasma concentration of venlafaxine over a twenty-four hour period with diminished fluctuations in blood drug concentration said method comprising administering orally to a patient in need thereof, a delayed burst release formulation comprising a core formed as a compressed tablet and an outer coating that surrounds the core; said core comprising venlafaxine, or a pharmaceutically acceptable salt thereof, at least one burst controlling agent and a disintegrant; and said outer coating comprising a water insoluble hydrophobic carrier and water-insoluble but hydrophilic particulate matter.

90. A method according to claim 89 wherein said formulation provides a delayed burst release after at least three hours resulting in dispersion of the active ingredient mainly through the colon into the blood stream as a result of colon absorption over a period of at least twenty-four hours.

91. A method for providing a therapeutic blood plasma concentration of venlafaxine over a twenty-four hour period with diminished side effects said method comprising administering orally to a patient in need thereof, a delayed burst release formulation comprising a core formed as a compressed tablet and an outer coating

that surrounds the core; said core comprising venlafaxine, or a pharmaceutically acceptable salt thereof, at least one burst controlling agent and a disintegrant; and said outer coating comprising a water insoluble hydrophobic carrier and water-insoluble but hydrophilic particulate matter.

92. A method according to claim 91 wherein said formulation provides a delayed burst release after at least three hours resulting in dispersion of the active ingredient mainly through the colon into the blood stream as a result of colon absorption over a period of at least twenty-four hours.

93. A method for obtaining improved patient compliance in venlafaxine usage comprising administering orally to a patient in need thereof, a delayed burst release formulation comprising a core formed as a compressed tablet and an outer coating that surrounds the core; said core comprising venlafaxine, or a pharmaceutically acceptable salt thereof, at least one burst controlling agent and a disintegrant; and said outer coating comprising a water insoluble hydrophobic carrier and water-insoluble but hydrophilic particulate matter.

(a) a core that comprises an effective amount of venlafaxine, wherein said core contains at least one burst controlling agent and a disintegrant, and wherein said core is formed as a compressed tablet; and

(b) an outer coating over said core, said outer coating comprising a water insoluble hydrophobic carrier and water-insoluble but hydrophilic particulate matter, contained in the carrier, that forms channels in said outer coating material upon contact with the colon medium, wherein said channels imbibe liquid and cause said at least one burst controlling agent to burst said coating, thereby providing delayed burst release of venlafaxine after at least three hours followed by dispersion of venlafaxine into the blood stream mainly through the colon over a period extending over at least twenty-four hours.